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CDPH Influenza Antiviral Guidance for Shelter Residents, December, 2018

The public health recommendations in this document are based on existing guidance regarding the use of antiviral medications for treatment and chemoprophylaxis of influenza in the general population and in long-term care facilities.^{1,2} The goals of this guidance are 1) to prevent morbidity due to influenza in shelter residents and 2) to prevent transmission of influenza among shelter residents, both by decreasing viral shedding by ill residents, and by protecting well contacts of influenza cases from influenza illness.

Influenza vaccination of shelter residents and staff and the prompt separation of those with influenza-like illness (ILI) from others remain the primary strategies for prevention of influenza in the shelter setting. Separation from others can be accomplished by spatial separation (Maintaining a distance of >6 feet, but no less than 3 feet, from other people and wearing a mask when within 6 feet of other people when masks are available) or by placement of ill residents in a respiratory isolation area.

This document does not replace clinical decision-making with respect to individual patient care. Residents who are clinically unstable should be transferred to a medical facility as soon as feasible.

Note: Influenza-like illness (ILI) is defined as fever (temperature of 100°F [37.8°C] or greater) and a cough and/or a sore throat in the absence of a KNOWN cause other than influenza. Individuals who are frail, elderly, and/or with weakened immune systems may be less likely to mount a fever, and clinical decision-making should be used regarding patients who do not meet all criteria for ILI but might have influenza.

¹ CDC. Antiviral Drugs – Information for Health Care Professionals.

<https://www.cdc.gov/flu/professionals/antivirals/index.htm>. Accessed 1 December 2018.

² California Department of Public Health. Recommendations for the Prevention and Control of Influenza in California Skilled Nursing Facilities (SNF), October, 2018.

https://www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/RecommendationsForThePreventionAndControlOfInfluenzaNov2018_FINAL.pdf



Oseltamivir is the first-line oral agent recommended for influenza antiviral treatment and chemoprophylaxis in the shelter setting. Note that treatment dosing differs from chemoprophylaxis dosing, and patients with impaired renal function require adjusted doses. Antiviral dosing tables are provided at the end of this document. Inhaled Zanamivir is an option for those who cannot receive oseltamivir. A new agent, baloxivir, has been approved for treatment of individuals 12 years and older; only a single dose is required for this drug.

Antiviral treatment for residents with influenza or ILI

- To decrease transmission of influenza, offer antiviral treatment promptly to shelter residents with laboratory-confirmed influenza or ILI pending laboratory confirmation, even individuals who are at low risk for complications. While treatment started within 48 hours of symptom onset is most effective, treatment started later can still be beneficial, especially for individuals at higher risk for severe illness and/or complications.
- Treatment is especially important for individuals who are at [high risk for complications of influenza](#), such as pregnant women and those who are immunocompromised, <2 years of age, or ≥65 years of age. (See CDC reference for complete list.)
- Because of the need for accurate diagnostic testing in the shelter setting, rapid influenza diagnostic tests (RIDTs) are not recommended due to their low sensitivity and specificity. Polymerase chain reaction (PCR) testing is recommended and is available at many clinical and public health laboratories.
 - Do not decide against or discontinue antiviral treatment based on a negative RIDT.
 - A negative RIDT result should be confirmed at a clinical or public health lab.
- Residents with influenza or ILI should be separated from others according to public health guidance, whether or not they are treated with antivirals. See “CDPH Infection Control Recommendations for Ambulatory Shelter Residents with Influenza-Like Illness, December 2018.”

Antiviral chemoprophylaxis for close contacts of residents with influenza or ILI

- In the shelter setting, close contacts are residents with beds within 6 feet of the ill resident’s bed, and family members or friends with whom the resident has had extensive face-to-face contact (such as eating meals or socializing together) from one day before symptom onset until separation from others was initiated.
- Antiviral chemoprophylaxis should be offered to close contacts of residents with influenza or ILI, whether or not they have received an influenza vaccine. Special consideration should be given to contacts who are at [high risk of influenza complications](#) due to age and/or underlying medical conditions. (See treatment and chemoprophylaxis dosing tables at the end of this document).
- Unvaccinated close contacts of residents with influenza or ILI should be offered influenza vaccine, whether or not they receive antivirals.

- Antiviral chemoprophylaxis should ideally be started within 48 hours of the most recent exposure to the ill individual. It should be continued for 10 days after the most recent exposure to the ill individual. Antiviral chemoprophylaxis should not be discontinued based on the ill resident testing negative on an RIDT. A negative RIDT result should be confirmed at a clinical or public health lab.
- Individuals receiving chemoprophylaxis should be instructed to report any symptoms of ILI to medical personnel. They should be informed that chemoprophylaxis lowers but does not eliminate the risk for influenza, and that susceptibility to influenza returns once the antiviral medication is stopped.
- Residents who develop influenza after taking antiviral chemoprophylaxis for 72 hours or more should be reported to the local health department so that the possibility of resistance to the antiviral agent used can be considered.

Antiviral chemoprophylaxis for healthcare personnel caring for shelter residents with influenza or ILI

- Unimmunized healthcare personnel who are providing care to shelter residents with influenza or ILI should be offered immunization and may be offered chemoprophylaxis.

Special circumstances

- If influenza activity in a specific shelter is unusually widespread, and if the population of the shelter predominantly consists of individuals at high-risk for complications, consideration may be given to offering chemoprophylaxis to a wider group of shelter residents. This decision would be made on a case-by-case basis in consultation with state and local public health authorities.

Table 1. Antiviral Medications Recommended for Treatment and Chemoprophylaxis of Influenza*

Antiviral Agent	Activity Against	Use	Recommended For	Not Recommended for Use in	Adverse Events
Oral Oseltamivir	Influenza A and B	Treatment	Any age ¹	N/A	Adverse events: nausea, vomiting, headache. Post marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events ²
		Chemo-prophylaxis	3 months and older ¹	N/A	
Inhaled Zanamivir	Influenza A and B	Treatment	7 yrs and older ³	people with underlying respiratory disease (e.g., asthma, COPD) ³	Adverse events: risk of bronchospasm, especially in the setting of underlying airways disease; sinusitis, and dizziness.. Post marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events ²
		Chemo-prophylaxis	5 yrs and older ³	people with underlying respiratory disease (e.g., asthma, COPD) ³	
Intravenous Peramivir	Influenza A and B ⁴	Treatment	2 yrs and older ⁴	N/A	Adverse events: diarrhea. Post marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events ²
		Chemo-prophylaxis ⁵	Not recommended	N/A	
Oral Baloxavir	Influenza A and B ⁶	Treatment	12 yrs and older ⁶	N/A	Adverse events: none more common than placebo in clinical trials
		Chemo-prophylaxis ⁵	Not recommended	N/A	

Abbreviations: N/A = not applicable, COPD = chronic obstructive pulmonary disease.

¹ Oral oseltamivir phosphate is approved by the FDA for treatment of acute uncomplicated influenza within 2 days of illness onset in people 14 days and older, and for chemoprophylaxis in people 1 year and older. Although not part of the FDA-approved indications, use of oral oseltamivir for treatment of influenza in infants less than 14 days old, and for chemoprophylaxis in infants 3 months to 1 year, is recommended by the CDC and the American Academy of Pediatrics. If a child is younger than 3 months old, use of oseltamivir for chemoprophylaxis is not recommended unless the situation is judged critical due to limited data in this age group.

² Self-injury or delirium; mainly reported among Japanese pediatric patients.

³ Inhaled zanamivir is approved by the FDA for treatment of acute uncomplicated influenza within 2 days of illness onset in people 7 years and older, and for chemoprophylaxis of influenza in people 5 years and older. Inhaled zanamivir is contraindicated in patients with history of allergy to milk protein.

⁴ Intravenous peramivir is approved by the FDA for treatment of acute uncomplicated influenza within 2 days of illness onset in people 2 years and older. Peramivir efficacy is based on clinical trials versus placebo in which the predominant influenza virus type was influenza A; in one trial, a very limited number of subjects infected with influenza B virus were enrolled.

⁵ There are no data for use of peramivir or baloxavir for chemoprophylaxis of influenza.

⁶ Oral baloxavir marboxil is approved by the FDA for treatment of acute uncomplicated influenza within 2 days of illness onset in people 12 years and older. The safety and efficacy of baloxavir for the treatment of influenza have been established in pediatric patients 12 years and older weighing at least 40 kg. Safety and efficacy in patients less than 12 years of age or weighing less than 40 kg have not been established. Baloxavir efficacy is based on clinical trials in outpatients 12 to 64 years of age; people with underlying medical conditions and adults >65 years and older were not included in the initial published clinical trials ([Hayden, 2018](#)). There are no available data for baloxavir treatment of hospitalized patients with influenza.

Table 2. Recommended Dosage and Duration of Influenza Antiviral Medications for Treatment or Chemoprophylaxis*

Antiviral Agent	Use	Children	Adults
Oral Oseltamivir	Treatment (5 days) ¹	If younger than 1 yr old²: 3 mg/kg/dose twice daily ^{3,4} If 1 yr or older, dose varies by child's weight: 15 kg or less, the dose is 30 mg twice a day > 15 to 23 kg, the dose is 45 mg twice a day > 23 to 40 kg, the dose is 60 mg twice a day > 40 kg, the dose is 75 mg twice a day	75 mg twice daily
	Chemo- prophylaxis (7 days) ⁵	If child is younger than 3 months old, use of oseltamivir for chemoprophylaxis is not recommended unless situation is judged critical due to limited data in this age group. If child is 3 months or older and younger than 1 yr old² 3 mg/kg/dose once daily ³ If 1 yr or older, dose varies by child's weight: 15 kg or less, the dose is 30 mg once a day > 15 to 23 kg, the dose is 45 mg once a day > 23 to 40 kg, the dose is 60 mg once a day > 40 kg, the dose is 75 mg once a day	75 mg once daily
Inhaled Zanamivir ⁶	Treatment (5 days)	10 mg (two 5-mg inhalations) twice daily (FDA approved and recommended for use in children 7 yrs or older)	10 mg (two 5-mg inhalations) twice daily
	Chemo- prophylaxis (7 days) ⁵	10 mg (two 5-mg inhalations) once daily (FDA approved for and recommended for use in children 5 yrs or older)	10 mg (two 5-mg inhalations) once daily
Intravenous Peramivir ⁷	Treatment (1 day) ¹	(2 to 12 yrs of age) One 12 mg/kg dose, up to 600 mg maximum, via intravenous infusion for a minimum of 15 minutes (FDA approved and recommended for use in children 2 yrs or older)	N/A
	Chemo- prophylaxis ⁸	Not recommended	(12 yrs and older) 40 to <80 kg: One 40 mg dose; ≥80 kg: One 80 mg dose ⁹

Oral Baloxavir ⁹	Treatment (1 day) ¹	FDA approved and recommended for use in children 12 yrs or older weighing at least 40 kg. See adult dosage.	(12 yrs and older) 40 to <80 kg: One 40 mg dose; ≥80 kg: One 80 mg dose ⁹
	Chemo- prophylaxis ⁸	Not recommended	N/A

Abbreviations: N/A = not applicable

¹Longer treatment duration may be needed for severely ill patients.

²Oral oseltamivir is approved by the FDA for treatment of acute uncomplicated influenza within 2 days of illness onset with twice-daily dosing in people 14 days and older, and for chemoprophylaxis with once-daily dosing in people 1 year and older. Although not part of the FDA-approved indications, use of oral oseltamivir for treatment of influenza in infants less than 14 days old, and for chemoprophylaxis in infants 3 months to 1 year of age, is recommended by the CDC and the American Academy of Pediatrics ([Committee on Infectious Diseases, 2018](#)).

³This is the FDA-approved oral oseltamivir treatment dose for infants 14 days and older and less than 1 year old, and provides oseltamivir exposure in children similar to that achieved by the approved dose of 75 mg orally twice daily for adults, as shown in two studies of oseltamivir pharmacokinetics in children ([Kimberlin, 2013 \[CASG 114\]](#), [EU study WP22849, FDA Clinical Pharmacology Review](#)). The American Academy of Pediatrics has recommended an oseltamivir treatment dose of 3.5 mg/kg orally twice daily for infants 9-11 months old, on the basis of data which indicated that a higher dose of 3.5 mg/kg was needed to achieve the protocol-defined targeted exposure for this cohort as defined in the CASG 114 study ([Kimberlin, 2013](#)). It is unknown whether this higher dose will improve efficacy or prevent the development of antiviral resistance. However, there is no evidence that the 3.5 mg/kg dose is harmful or causes more adverse events to infants in this age group.

⁴Current weight-based dosing recommendations are not appropriate for premature infants. Premature infants might have slower clearance of oral oseltamivir because of immature renal function, and doses recommended for full-term infants might lead to very high drug concentrations in this age group. CDC recommends dosing as also recommended by the American Academy of Pediatrics ([Committee on Infectious Diseases, 2018](#)): limited data from the National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group provide the basis for dosing preterm infants using their postmenstrual age (gestational age + chronological age): 1.0 mg/kg/dose, orally, twice daily, for those <38 weeks postmenstrual age; 1.5 mg/kg/dose, orally, twice daily, for those 38 through 40 weeks postmenstrual age; 3.0 mg/kg/dose, orally, twice daily, for those >40 weeks postmenstrual age.

⁵See Special Considerations for Institutional Settings section below for details regarding duration of chemoprophylaxis for outbreaks in institutional settings.

⁶Inhaled zanamivir is approved for treatment of acute uncomplicated influenza within 2 days of illness onset with twice-daily dosing in people 7 years and older, and for chemoprophylaxis with once-daily dosing in people 5 years and older.

⁷Intravenous peramivir is approved for treatment of acute uncomplicated influenza within 2 days of illness onset with a single dose in people 2 years and older. Daily dosing for a minimum of 5 days was used in clinical trials of hospitalized patients with influenza ([de Jong, 2014](#), [Ison, 2014](#)).

⁸There are no data for use of peramivir or baloxavir for chemoprophylaxis of influenza.

⁹Oral baloxavir is [approved for treatment of acute uncomplicated influenza within 2 days of illness onset with a single dose in people 12 years and older who weigh more than 40 kg](#) (Hayden, 2018). Safety and efficacy in patients less than 12 years old or weighing less than 40 kg have not been established. Baloxavir marboxil should not be administered with dairy products, calcium-fortified beverages, polyvalent cation-containing laxatives, antacids or oral supplements (e.g., calcium, iron, magnesium, selenium, or zinc); co-administration with polyvalent cation-containing products may decrease plasma concentrations of baloxavir, which may reduce efficacy.

Table 3. Recommended Oseltamivir and Peramivir Dose Adjustments for Treatment or Chemoprophylaxis of Influenza in Adult Patients with Renal Impairment or End Stage Renal Disease (ESRD) on Dialysis*†

Creatinine Clearance		Recommended Treatment Regimen	Recommended Chemoprophylaxis Regimen
Oral oseltamivir¹	Creatinine clearance 61 to 90 mL/min	75 mg twice a day	75 mg once daily
	Creatinine clearance 31 to 60 mL/min	30 mg twice a day	30 mg once daily
	Creatinine clearance 11 to 30 mL/min	30 mg once daily	30 mg every other day
	ESRD Patients on Hemodialysis Creatinine clearance ≤10 mL/min	30 mg after every hemodialysis cycle. Treatment duration not to exceed 5 days ²	30 mg after alternate hemodialysis cycles ³
	ESRD Patients on Continuous Ambulatory Peritoneal Dialysis ⁴ Creatinine clearance ≤10 mL/min	A single 30 mg dose administered immediately after a dialysis exchange	30 mg once weekly immediately after dialysis exchange
Intravenous Peramivir (single dose)⁵	Creatinine clearance ≥50 mL/min	600 mg	N/A
	Creatinine clearance 30 to 49 mL/min	200 mg	N/A
	Creatinine clearance 10 to 29 mL/min	100 mg	N/A
	ESRD Patients on Hemodialysis	Dose administered after dialysis at a dose adjusted based on creatinine clearance	

†From package inserts for oseltamivir and peramivir; see [FDA Influenza \(Flu\) Antiviral Drugs and Related Information](#).

Abbreviations: N/A = not applicable

¹Renal dosing of oseltamivir is not available in the [package insert](#) for pediatric patients. However, these tables may be useful for children who qualify for adult doses based on weight >40 kg.

²Assuming 3 hemodialysis sessions are performed in the 5- day period. Treatment can be initiated immediately if influenza symptoms develop during the 48 hours between hemodialysis sessions; however, the post-hemodialysis dose should still be administered independently of time of administration of the initial dose.

³An initial dose can be administered prior to the start of dialysis.

⁴Data derived from studies in continuous ambulatory peritoneal dialysis (CAPD) patients.

⁵Renal dosing from [peramivir package insert](#) is available for pediatric patients: Creatinine clearance ≥50 mL/min: 12 mg/kg (up to maximum dose of 600 mg); Creatinine clearance 30 to 49 mL/min: 4 mg/kg; Creatinine clearance 10 to 29 mL/min: 2 mg/kg.

*CDC. Influenza Antiviral Medications: Summary for Clinicians <https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>